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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,100	11/12/2003	Seymour H. Fein	102463-201	7710

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WIGGIN AND DANA LLP
ATTENTION: PATENT DOCKETING
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EXAMINER	
TATE, CHRISTOPHER ROBIN	
ART UNIT	**PAPER NUMBER**
1655	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/706,100	FEIN, SEYMOUR H.	
	Examiner	Art Unit	
	Christopher R. Tate	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,7,9,27 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1, 3, 4, 6, 7, 9, 27, and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1206*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 26 December 2006 is acknowledged and has been entered. Claims 1, 3, 4, 6, 7, 9, 27, and 28 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1, 3, 4, 6, 7, 9, 27, and 28 stand/are rejected under 35 U.S.C. 102(b) as being anticipated by Yiv (US 5,707,648).

A pharmaceutical composition in a dosage form adapted for intranasal, transmucosal, transdermal, conjunctival, or intradermal administration comprising 0.5 ng to 20 *u*g (and narrower ranges) of desmopressin is claimed.

Yiv teaches pharmaceutical compositions comprising desmopressin within the instantly claimed amount ranges - including within gelatin filled capsules for peroral administration (please note that such capsules read upon a form adapted for "transmucosal" administration - as instantly claimed), within a drug delivery formulation as shown in Example 6c, as well as within a liquid formulation for subcutaneous injectable administration. For example, Yu discloses capsules containing 13 *u*g and capsules containing 43 *u*g desmopressin, a drug delivery formulation containing 18 *u*g/g desmopressin - as shown in Example 6c, and subcutaneous injectable formulations containing 0.4 *u*g/ml desmopressin (so as to provide 4 *u*g/kg body weight thereof) - see, e.g., col 15, line 62 - col 18, line 26. Please note that the discussed desmopressin pharmaceutical compositions of the cited reference read upon a dosage form adapted for one or

more of the administrative means instantly claimed (including, e.g., adapted so as to be suitable for being added to an intranasal, transmucosal, transdermal, conjunctival, and/or intradermal formulation/patch - i.e., the desmopressin forms taught by Yiv (e.g., within a capsule, injectable, and/or other drug delivery formulation) are suitable (and thus "adapted for" use) in transmucosal, transdermal, conjunctival, and/or intradermal administrative formulations (as instantly claimed). In addition, please note the above discussed desmopressin formulations taught by Yiv would inherently provide the instantly claimed functional effect upon administration - i.e., if the desmopressin formulations taught by the Yiv were administered (or if they were administered in a form adapted for intranasal, transmucosal, transdermal, conjunctival, and/or intradermal administration), a steady plasma/serum desmopressin concentration within the approximate instantly claimed range, as well as a decrease in urine production, would inherently occur (especially given that the amounts of desmopressin within the referenced desmopressin formulations are within the instantly claimed amount ranges).

Therefore, the reference is deemed to anticipate the instantly claimed invention.

Claims 1, 3, 7, 9, 14, 27, and 28 stand/are rejected under 35 U.S.C. 102(e) as being anticipated by Alonso et al. (US 6,693,082).

Alonso et al. teach pharmaceutical compositions comprising desmopressin within the instantly claimed amount ranges. For example, Alonso et al. teach an intravenous pharmaceutical composition comprising a dose of lower than 20 *u*g (but higher than the instantly claimed lower ng amount) and pharmaceutical compositions comprising 1-2 *u*g/kg of body weight doses of desmopressin (dissolved in 50-100 ml saline for injectable infusion) - see, e.g.,

col 9, line 54 - col 10, line 45, and claims. Alonso et al. also disclose conventional prior art desmopressin pharmaceutical compositions comprising 4 *u*g/ml desmopressin packaged within ampoules (see, e.g., col 8, lines 35-49). Please note that the discussed desmopressin pharmaceutical compositions of the cited reference read upon a dosage form adapted for one or more of the administrative means instantly claimed (including, e.g., adapted so as to be suitable for being added to an intranasal, transmucosal, transdermal, conjunctival, and/or intradermal formulation/patch - i.e., the desmopressin forms taught by Alonso et al. are suitable (and thus "adapted for" use) in transmucosal, transdermal, conjunctival, and/or intradermal administrative formulations (as instantly claimed). In addition, please note the above discussed desmopressin formulations taught by Alonso et al. would inherently provide the instantly claimed functional effect upon administration - i.e., if the desmopressin formulations taught by Alonso et al. were administered (or if they were administered in a form adapted for intranasal, transmucosal, transdermal, conjunctival, and/or intradermal administration), a steady plasma/serum desmopressin concentration within the approximate instantly claimed range, as well as a decrease in urine production, would inherently occur (especially given that the amounts of desmopressin within the referenced desmopressin formulations are within the instantly claimed amount ranges).

Therefore, the reference is deemed to anticipate the instant claims above.

Claims 1, 3, 7, 9, 14, 27, and 28 stand/are rejected under 35 U.S.C. 102(e) as being anticipated by Shapiro (US 6,746,678).

Shapiro discloses a commercial pharmaceutical composition (packaged within a nasal spray applicator) comprising desmopressin at a daily dosage concentration of 10 *u*g.- see, e.g., col 53, lines 9-11 (please note that such a form would inherently be in the form of a solution). Please note that the discussed desmopressin pharmaceutical composition of the cited reference reads upon a dosage form adapted for one or more of the administrative means instantly claimed (including, e.g., adapted so as to be suitable for being added to an intranasal, transmucosal, transdermal, conjunctival, and/or intradermal formulation/patch - i.e., the desmopressin form (intranasal solution) taught by Shapiro is suitable (and thus "adapted for" use) in transmucosal, transdermal, conjunctival, and/or intradermal administrative formulations (as instantly claimed). In addition, please note the above discussed desmopressin formulation taught by Shapiro would inherently provide the instantly claimed functional effect upon administration - i.e., if the desmopressin formulation taught by Shapiro was administered (or if it was administered in a form adapted for intranasal, transmucosal, transdermal, conjunctival, and/or intradermal administration), a steady plasma/serum desmopressin concentration within the approximate instantly claimed range, as well as a decrease in urine production, would inherently occur (especially given that the amount of desmopressin within the referenced desmopressin formulations are within the instantly claimed amount ranges).

Therefore, the reference is deemed to anticipate the instant claims above.

Claims 1, 5-7, 9, 27, and 28 stand/are rejected under 35 U.S.C. 102(b) as being anticipated by Stanley et al. (US 4,863,737).

Stanley et al. teach a pharmaceutical composition (in the form of a lollipop, which reads upon an a dosage form "adapted for transmucosal administration" - as instantly claimed) comprising 20 *u*g of desmopressin therein (see, e.g., col 24, lines 40-61 - Example 20). In addition, please note the above discussed desmopressin formulation taught by Shapiro would inherently provide the instantly claimed functional effect upon administration - i.e., if the desmopressin formulation taught by Shapiro was administered (or if it was administered in a form adapted for intranasal, transmucosal, transdermal, conjunctival, and/or intradermal administration), a steady plasma/serum desmopressin concentration within the approximate instantly claimed range, as well as a decrease in urine production, would inherently occur (especially given that the amount of desmopressin within the referenced desmopressin formulations are within the instantly claimed amount ranges).

Therefore, the reference is deemed to anticipate the instant claims above.

Claims 1, 3-5, 7, 9, 27, and 28 stand/are rejected under 35 U.S.C. 102(b) as being anticipated by Trinh-Trang-Tan et al. (J. Am. Soc. Nephrol., 2000 - BIOSIS Meeting Abstract), by Wolfson et al. (Am. J. Gastroenterol., 1979), by Jahr et al. (Anesthesia & Analgesia, 1992), by Dixon et al. (Br. J. Radiol., 1981), by Malan et al. (Toxicol. Methods, 1994), or by Tormey et al. (Eur. J. Internal Med., 1992).

Each of the cited references teaches pharmaceutical composition (in liquid form) comprising desmopressin within the instantly claimed amount ranges (see entire documents). Please note that each of the referenced desmopressin pharmaceutical compositions read upon a dosage form adapted for one or more of the administrative means instantly claimed (including,

e.g., adapted so as to be suitable for being added to an intranasal, transmucosal, transdermal, conjunctival, and/or intradermal formulation/patch - i.e., the desmopressin forms taught by each of the cited references are suitable (and thus "adapted for" use) in transmucosal, transdermal, conjunctival, and/or intradermal administrative formulations (as instantly claimed). In addition, please note the above discussed desmopressin formulations taught by each of the cited references would inherently provide the instantly claimed functional effect upon administration - i.e., if the desmopressin formulations taught by each of the cited references were administered (or if they were administered in a form adapted for intranasal, transmucosal, transdermal, conjunctival, and/or intradermal administration), a steady plasma/serrum desmopressin concentration within the approximate instantly claimed range, as well as a decrease in urine production, would inherently occur (especially given that the amounts of desmopressin within each of the referenced desmopressin formulations are within the instantly claimed amount ranges).

Therefore, each of the cited references is deemed to anticipate the instant claims above.

With respect to each of the USC 102 rejections above - it is reemphasized that, although Applicant is claiming a pharmaceutical product (not a method of its use), the administration of the cited prior art desmopressin pharmaceutical compositions (and/or the administration of the cited prior art desmopressin pharmaceutical compositions in a form adapted for intranasal, transmucosal, transdermal, conjunctival, and/or intradermal administration) would inherently provide the instantly claimed intended (post-administered) functional effect (i.e., "establish a steady plasma/serum desmopressin concentration" within the instantly claimed approximate picogram ranges as well as "decrease urine production" in an administered subject).

Applicant's arguments concerning the above USC 102 rejections have been carefully considered but are not deemed to be persuasive of error in the rejections. Applicant argues at the outset that the Examiner's position that the administration of the cited prior art desmopressin pharmaceutical compositions would inherently provide the instantly claimed function effect (i.e., establishing a steady state plasma/serum desmopressin concentration) is incorrect because the claims require that concentrations within this range must be established, that is, maintained for some reasonable time, and that underlying the instantly claimed invention is the discovery that maintenance of such low doses can act effectively to interrupt urine production while decreasing or eliminating induction of hyponatremia. However, as discussed above, the claims are all drawn to a pharmaceutical product (not to a method of its use) and, as such, the prior art references (whereby the amounts of desmopressin within the cited reference pharmaceutical compositions are within the approximate amount ranges instantly claimed) read upon the instantly claimed pharmaceutical product. Throughout the reply filed 26 December 2006, Applicant repeatedly argues that the prior art references do not teach or recognize that their desmopressin pharmaceutical compositions can provide the instantly claimed *in vivo* functional effects (upon administration thereof). For example, Applicant argues that Yiv discloses an oral (capsule) dosage as well as a subcutaneous dosage, and that Alonso et al. teach an intravenous dosage; but there is no recognition in the prior art for the instantly claimed *in vivo* functional effects upon administration thereof. However, as discussed above, please note the above discussed desmopressin formulations taught by each of the cited references would inherently provide the instantly claimed functional effect upon administration - i.e., if the desmopressin formulations taught by each of the cited references were administered (or if they were

administered in a form adapted for intranasal, transmucosal, transdermal, conjunctival, and/or intradermal administration), a steady plasma/serum desmopressin concentration within the approximate instantly claimed range, as well as a decrease in urine production, would inherently occur (especially given that the amounts of desmopressin within each of the referenced desmopressin formulations are within the approximate amount ranges instantly claimed).

Claim Rejections - 35 USC § 103

Claim 1, 3, 4, 6, 7, 9, 27, stand/and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yiv (US 5,707,648) and Stanley et al. (US 4,863,737).

The Yiv reference is relied upon for the reasons discussed *supra*. Yiv further beneficially teach the use of soft or hard gelatin capsules as well as starch capsules for effective (preferably oral) administration of such protein-containing formulations, and that preparing such hard and soft gelatin capsules is routine and well known in the art (based upon the incorporation therein of prior art pharmacy text teachings). Yiv also teaches that a particularly preferable and useful protein to incorporate within such capsules is desmopressin. (see entire document including Abstract; col 3, line 46 - col 4, line 15; col 6, line 67 - col 7, line 20; col 8, lines 9-32; col 10, lines 25-36; col 14, lines 38-65).

Stanley et al. teach a pharmaceutical composition (in the form of a lollipop, which reads upon a dosage form adapted for "transmucosal administration" - as instantly claimed) comprising 20 *u*g of desmopressin therein (see, e.g., col 24, lines 40-61 - Example 20) as an effective oral delivery form. In addition, Stanley et al. beneficially teach employing a desmopressin dosage range of 10 to 50 *u*g within such solid confectionary/candy matrix orally-administered products (see, e.g., col 17, lines 21-23).

It would have been obvious to one of ordinary skill in the art to incorporate the instantly claimed amount ranges (as best understood) of desmopressin within an oral formulation including within a hard or soft gelatin or starch capsule, and/or within a solid confectionary/candy (such as a lollipop) - so as to provide effective oral delivery pharmaceutical forms thereof, based upon the overall beneficial teachings provided by the cited references, as discussed above. The result-effective adjustment of particular conventional working conditions (e.g., employing a conventional routinely-employed rapid-dissolving gelatin or starch capsule in the pharmaceutical capsule preparations disclosed by Yiv, and/or encasing a candy including a lollipop such as disclosed by Stanley et al. within a candy wrapper and an outer box/container to protect the integrity of the candy/lollipop product as well as to provide it in a form acceptable for commercial vending sale - which would read upon "an article of manufacture" in which the desmopressin pharmaceutical composition is packaged therein) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. Please note that the administration of such prior art desmopressin pharmaceutical compositions would intrinsically provide the instantly claimed intended functional effect (i.e., "to establish a steady plasma/serum desmopressin concentration" in the approximate picogram ranges and "to decrease urine production" - as instantly claimed).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments concerning the above USC 103 rejection has been carefully considered but are not deemed to be persuasive of error in the rejection. Applicant argues that the properties and advantages of a chemical composition are part of the subject matter taken as a whole and, therefore, the pharmaceutical composition as claimed cannot fairly be rejected as obvious because it addresses and solves a problem not so much as appreciated by the applied references, namely, how to safely interrupt urine production in adults, particularly without substantial risk of hyponatremia - which Yiv and Stanley et al. do not teach or suggest. Applicant further argues that neither reference teach or suggest the use of lower dosages, much less that such lower dosages are effective to interrupt urine production while avoiding hyponatremia. However, as discussed above, the claims are all drawn to a pharmaceutical product (not to a method of its use) and, as such, the prior art references (whereby the amounts of desmopressin within the cited reference pharmaceutical compositions are within the approximate amount ranges instantly claimed) reasonably read upon the instantly claimed pharmaceutical product. Further, as discussed above, please again note the above discussed desmopressin formulations taught and/or reasonably suggested by the cited references would intrinsically provide the instantly claimed functional effect upon administration - i.e., if the desmopressin formulations taught or reasonably suggested by the cited references were administered (or if they were administered in a form adapted for intranasal, transmucosal, transdermal, conjunctival, and/or intradermal administration), a steady plasma/serrum desmopressin concentration within the approximate instantly claimed range, as well as a decrease urine production, would intrinsically occur (especially given that the amounts of desmopressin taught and/or suggested by

the referenced desmopressin formulations are within the approximate amount ranges instantly claimed).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Tate whose telephone number is (571) 272-0970. The examiner can normally be reached on Mon-Thur, 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher R. Tate
Primary Examiner
Art Unit 1655